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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,765	11/08/2001	Preben Christensen	60123.000002	4417

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HUNTON & WILLIAMS LLP
INTELLECTUAL PROPERTY DEPARTMENT
1900 K STREET, N.W.
SUITE 1200
WASHINGTON, DC 20006-1109

EXAMINER

SAUCIER, SANDRA E

ART UNIT

PAPER NUMBER

1651

DATE MAILED: 11/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/914,765	Applicant(s) CHRISTENSEN ET AL.	
	Examiner Sandra Saucier	Art Unit 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 September 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-11,14-45 and 49 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-11,14-45 and 49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 05 September 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>2/27/04, 9/27/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1, 3-11, 14-45 and 49 are pending and are considered on the merits.

Claim Rejections – 35 USC § 102

Claims 1, 3, 5, 6, 9, 31, 45 and 49 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Yamamoto *et al.* [28].

The claims are directed to a method of determining absolute sperm concentration and % viability in a semen sample comprising selective staining and determining the absolute concentration of sperm and the proportion of live sperm in the semen sample simultaneously.

Yamamoto *et al.* disclose a method to determine sperm number and sperm viability using PI and FCM. The semen is weighed and mixed with determined volume of D-PBS, PI added to the sample and analysis of a determined volume is by FCM. The total number of sperm and the dead sperm are both counted at the same time. The number of sperm in the semen was then calculated to be 1.28×10^6 /mg semen with a 78% viability.

Claims 1, 3-10, 16-19, 28, 31, 45, 49 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by US 4,559,309 [B].

US 4,559,309 states that "Major criteria for clinical evaluation of semen samples include: (1) sperm number, (2) sperm viability... and that parameters 1-3 can be determined from a single FCM measurement using R123/EB staining..." (column 8, lines 11-16). The reference also states that the diluent can contain FBS and implies that the staining is done at room temperature since no other temperature is mentioned.

Claims 1, 3, 5-9, 20-24, 28, 29, 31, 45 and 49 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Takizawa *et al.* [22].

Takizawa *et al.* obtain a semen sample, dilute with D-PBS, BSA, add PI and fluorescent beads (Immuno-check) as an internal standard and analyze for dead, dying and viable sperm as well as absolute concentration (page 178, 179 and second paragraph on page 180). These determinations are done in one pass on the FACScan as stated on page 180.

Claim Rejections – 35 USC § 103

Claims 1, 3-11, 14-24, 28, 29, 31, 37, 44, 45, 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takizawa *et al.* [22] in view of Live/Dead Sperm Viability Kit [U1] or Garner *et al.* [8]

The claimed method has been discussed above.

The references are relied upon as explained below.

Takizawa *et al.* obtain a semen sample, dilute with D-PBS, BSA, add PI and fluorescent beads (Immuno-check) as an internal standard and analyze for dead, dying and viable sperm as well as absolute concentration (page 178, 179 and second paragraph on page 180). These determinations are done in one pass on the FACScan as stated on page 180.

Live/Dead Sperm Viability Kit discloses a method of determining the proportion of live sperm cells in a sample by staining with SYBR 14 and propidium iodide and analyzed by flow cytometry. The diluent contain BSA.

Garner *et al.* teach a method of viability determination of freshly diluted or cryopreserved sperm using SYBR-14 and PI.

The substitution of two distinct fluorescent dyes for the PI in the method of Takizawa *et al.* would have been obvious when the primary reference was taken with Garner *et al.* or Live/Dead Sperm Viability Kit which both teach the superiority of their dual staining method to determine sperm viability.

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With regard to the use of a 25–75nM concentration of fluorochrome stain, Live/Dead Sperm Viability Kit states in the staining protocol that the examples are provided to guide researchers in the development of their own staining protocol, and that concentrations of reagents required for optimal staining may vary depending on density and other materials in the sperm sample. 100nM SYBR 14, used in the example, is the highest concentration recommended. In the absence of evidence to the contrary, given the guidance in the prior art, one of skill in the art may optimize the concentration required.

With regard to the temperature of incubation, Garner *et al.* and Sperm Viability Kit teach 36°C for 5–15 minutes. The protocol in the Viability Kit is provided to guide researchers in the development of their own staining protocol. In the absence of criticality, the use of lower temperatures is well within the purview of one of ordinary skill in the art as suggested by the Viability Kit.

Claim 25–27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takizawa *et al.* [22] and Live/Dead Sperm Viability Kit [U] or Garner *et al.* [8] as applied to claims 1, 3–11, 14–24, 28, 29, 31, 37, 44, 45, 49 above and in combination with EP 0 586 183 [I].

EP 586 183 discloses a method of determining absolute cell counts in a sample using a known number of fluorescent particles added to a known volume of sample, and using a flow cytometer (Summary of the Invention). Also disclose is a preferred 1/1 ration of fluorescent beads to cells for precise counting (page 5).

With regard to the number of fluorescent beads per sperm cell used in Takizawa *et al.* do not disclose the number of beads in 100microliters of Immuno-Check™. However, EP 0 586 183 discloses guidelines for the number of beads/number of cells deemed to be advantageous in flow cytometry for determination of absolute numbers of cells. This is generally near a 1/1 ratio (page 5, l. 35). In the absence of evidence to the contrary, the reference of

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Takizawa *et al.* is assumed to use this well-known relationship of fluorescent particles to cells for the most precise count.

Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Takizawa *et al.* [22] and Live/Dead Sperm Viability Kit [U] or Garner *et al.* [8] as applied to claims 1, 3-11, 14-24, 28, 29, 31, 37, 44, 45, 49 above, and further in view of Clay *et al.* [W1].

The claim is further directed to the addition of PVA to the dilution medium.

Clay *et al.* teach that decrease in sperm motility due to dilution may be reduced by the addition of PVA or BSA, abstract.

The addition of PVA or the substitution of PVA for BSA in the dilution medium in the methods of Takizawa *et al.* in combination with Live/Dead Sperm Viability Kit or Garner *et al.* would have been obvious when taken with Clay *et al.* who teach the advantages of such an addition.

Claims 32-34, 39, 41, 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takizawa *et al.* [22], Live/Dead Sperm Viability Kit [U1] or Garner *et al.* [8] as applied to claims 1, 3-11, 14-24, 28, 29, 31, 37, 44, 45, 49 above, and further in view of Sexton [X1] or Januskauskas *et al.* [U2] or Belorkar *et al.* [V2] or Bostofte *et al.* [W2]

The claims are further directed to the use of the determination of the concentration and proportion of viable sperm in the sample to predict fertility and as a basis to adjust AI dosage.

Sexton teach that concentration and viability of sperm in an insemination dosage are directly correlated to fertility for turkey semen. Sexton also teach the use of determination of the concentration of viable sperm to adjust the insemination dosage in order to obtain high fertility rates.

Januskauskas *et al.* teach that membrane integrity (viability) and concentration of sperm from a cryopreserved sample is directly correlated with fertility in bulls.

Belorkar *et al.* teach that sperm concentration and viable sperm % are directly correlated with fertility in bulls in fresh ejaculates.

Bostofte *et al.* teach that semen quality is a function of sperm count (concentration) and viability and that semen quality is directly correlated with fertility in humans.

The prediction of fertility based on a determination of sperm concentration and viability which is determined by prior art methods as demonstrated above would have been obvious because many in the art have shown a direct correlation between sperm concentration and sperm viability with fertility.

Claims 35 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takizawa *et al.* [22] Live/Dead Sperm Viability Kit [U1] or Garner *et al.* [8] as applied to claims 1, 3-11, 14-24, 28, 29, 31, 37, 44, 45, 49 above, and further in view of Juonala *et al.* [X2] and/or Viudes-De-Castro *et al.* [U3].

Juonala *et al.* disclose that sperm viability is directly correlated with fertility which is measured by non-return rates and litter size.

Viudes-De-Castro *et al.* disclose that sperm concentration has a direct correlation with fertility and litter size up to a threshold value.

The prediction of litter size which is correlated with fertility and predicted in the prior art by determination of sperm viability and sperm concentration would have been obvious because Juonala *et al.* have shown a direct correlation between sperm viability with fertility, of which litter size is an element and

Viudes-De-Castro *et al.* have demonstrated a direct correlation of litter size with sperm concentration up to a threshold value.

One of ordinary skill in the art would have been motivated at the time of invention to make these substitutions in order to obtain the results as suggested by the references with a reasonable expectation of success. The claimed subject matter fails to patentably distinguish over the state of the art as represented by the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

In short, the staining method, and the counting method with an addition of an internal standard and use to which the results, namely sperm concentration and viability, are employed are all known in the art and the combination of these methods is not unobvious especially because it is known that fertility is correlated with absolute sperm count as well as with viability of the sperm.

Response to Arguments

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, all references are directed to the same scientific area and are published prior to the effective filing date of the instant application. Thus, this knowledge is generally available to one of ordinary skill in the art.

The declaration filed has been carefully considered. While the precision of treatment C in the declaration is impressive, the method in the declaration is not the same method as now being claimed.

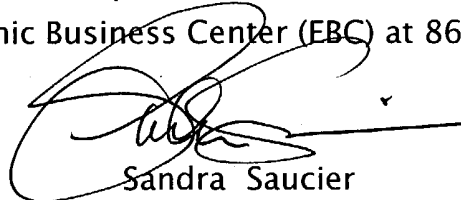
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The evidence relied upon should also be reasonably commensurate in scope with the subject matter claimed and illustrate the claimed subject matter "as a class" relative to the prior art subject matter "as a class." In re Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971); In re Hostettler, 429 F.2d 464, 166 USPQ 558 (CCPA 1970). See, also, In re Lindner, 457 F.2d 506, 173 USPQ 356 (CCPA 1972). Particularly, in the instant case, the scope of the claims is not commensurate with the showing. Narrowing of the claimed method may advance prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Saucier whose telephone number is (571) 272-0922. The examiner can normally be reached on Monday, Tuesday, Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, M. Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Sandra Saucier

Primary Examiner

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